Wnt/Catenin Signaling in Adult Stem Cell Physiology and Disease.

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Public Summary:
The article represents a literature review that summarizes current knowledge on the role of Wnt/catenin signaling, a highly conserved developmental pathway, in stem cells biology. In particular, the article focuses on current knowledge about its role in adult stem cells in body homeostasis as well as cancer etiology. We describe the importance of Wnt signaling in various organ systems, focusing on the role of two pivotal transcriptional co-activators of Wnt/catenin signaling, namely CBP and p300, in coordinating stem cell biology in physiology and disease. Furthermore, we are discussing the role chemical small molecules can play in orchestrating Wnt/catenin signaling and how this could be of potential benefit for regenerative medicine and novel strategies in cancer therapy.

Scientific Abstract:
Wnt signaling plays an important role in development and disease. In this review we focus on the role of the canonical Wnt signaling pathway in somatic stem cell biology and its critical role in tissue homeostasis. We present current knowledge how Wnt/beta-catenin signaling affects tissue stem cell behavior in various organ systems, including the gut, mammary gland, the hematopoietic and nervous system. We discuss evidence that canonical Wnt signaling can both maintain potency and an undifferentiated state as well as cause differentiation in somatic stem cells, depending on the cellular and environmental context. Based on studies by our lab and others, we will attempt to explain the dichotomous behavior of this signaling pathway in determining cell fate decisions and put special emphasis on the interaction of beta-catenin with two highly homologous co-activator proteins, CBP and p300, to shed light on the their differential role in the outcome of Wnt/beta-catenin signaling. Furthermore, we review current knowledge regarding the aberrant regulation of Wnt/beta-catenin signaling in cancer biology, particularly its pivotal role in the context of cancer stem cells. Finally, we discuss data demonstrating that small molecule modulators of the beta-catenin/co-activator interaction can be used to shift the balance between undifferentiated proliferation and differentiation, which potentially presents a promising therapeutic approach to stem cell based disease mechanisms.